None of the cited references describe the batch process claimed by the present invention and, therefore, do not anticipate the present invention. Specifically, WO '061 nowhere describes a solution concentration of 6-APA lower than 300 mM. Similarly, WO '420, nowhere describes the combined concentration of 6-APA and ampicillin being greater than 250 mM, or the solution concentration of 6-APA being lower than 300 mM.

WO '663 describes a continuous process, as opposed to batch process of the present invention, with no mention of features (i) – (iii) of instant claim 1. For example, Example 11, as cited by the Examiner as evidence of anticipation, describes a concentration of 6-APA of 200 mM, which obviously is below the claimed limitation of "greater than 250 mM." Without responding to the merits of the Examiner's argument presented on page 3 of paper 9, the Applicants note that even if, *in arguendo*, the Examiner where correct in his assumption of phenylglycine derative APA ratios, he has not shown how all the features of the instant invention have been anticipated by this reference. Finally, the Applicants note the Examiner has acknowledged on page 4 of paper 9, that this reference is directed to a continuous process and not a batch one, before describing how such a jump from continuous to batch would have been *obvious*.

Accordingly, withdrawal of these §102 rejections is respectfully requested.

The Applicants note that no proper case of *prima facie* obviousness has been established in the record, and therefore request withdrawal of this rejection. Specifically, no argument has been made of record establishing the motivation to

obtain the claimed invention from the prior art; that all of the claimed invention's limitations may be found within or readily suggested from the prior art; or that there was a reasonable expectation of successfully obtaining the claimed invention from the teachings of the prior art.

WO '061 is silent on the benefits in conversion seen with a phenylglycine derivative APA ratio of less than 2.5. Furthermore the Examples of this reference show much higher ratios (e.g., 7) and that yields for these systems were higher than for lower phenylglycine derivative APA ratios such as 2.7. Accordingly the skilled artisan would find no motivation to obtain the improved conversions of the present invention by looking to WO '061 because this reference suggests higher phenylglycine derivative APA ratios are advantageous.

With regard to WO '420, the Applicants note that this reference is directed to recovering the phenylglycine derivative from the reaction mixture and not to improving the reaction conversions. This fact alone provides shows that WO '420 is an unlike source of motivation to obtain the present invention. Still further, this reference teaches the concentrations of reactants used by this process *are not critical*. See Page 1, lines 10-15. Thus the skilled artisan is afforded no reasonable expectation of success in obtaining better reaction conditions by the general reagent recovery technique described by this reference.

Finally the Applicants note that WO '663 also fails to render the present invention obvious. In addition to being limited to a *continuous* process, in contrast to the presently claimed *batch* process, this reference provides no motivation to the

skilled artisan to use total concentrations of 6-APA and ampicillin greater than 250 mM, while maintaining a solution concentration of 6-APA lower than 300 mM. Accordingly, the Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

In view of the above amendments to the claims and the foregoing remarks, the Applicants respectfully assert that all of the Examiner's objections and rejections have been overcome. Accordingly, early and favorable notice of allowance of the present application is respectfully requested.

Respectfully submitted,

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Enclosure:
Appendix

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

1. (Twice Amended) A batch process for preparation of ampicillin comprising:

a) **[subjecting]** acylating 6-aminopenicillanic acid (6-APA) **[to an enzymatic acylation reaction with the aid of]** with a phenylglycine derivative in the presence of an enzyme to form a reaction mixture; **[,]**

wherein:

i) **[with]** the total concentration of **[the]** 6-APA and ampicillin combined **[present in the reaction mixture, plus ampicillin, being]** is greater than 250 mM; **[,]**

ii) the concentration of 6-APA in solution **[being kept]** is lower than 300 mM; and

iii) the molar ratio of **[acylating agent to 6-APA employed, which molar ratio is defined as]** the total quantity of added phenylglycine derivative **[divided by the total quantity of added]** to the total quantity of added 6-APA **[, expressed in moles, being]** is less than 2.5.

4. (Twice Amended) Process according to Claim 1, wherein the molar ratio of the total **[acylating agent]** phenylglycine derivative employed to 6-APA is less than 2.0

9. (Twice Amended) Process according to Claim 1, wherein the pH of the reaction mixture is lowered **[as soon as near to maximum conversion is achieved]**.

10. (Twice Amended) Process according to Claim 1, wherein the temperature of the reaction mixture is lowered **[as soon as near maximum conversion is achieved]**.